CLAIMS

1. An isolated polypeptide having the sequence recited in SEQ ID NO:16 or a variant thereof that differs in one or more amino acid deletions, insertions or substitutions at no more than 15% of the residues in SEQ ID NO: 16, such that the polypeptide enhances ubiquitination of phosphorylated IκB.

2. An isolated polypeptide comprising a portion of a human E3 ubiquitin, ligase recited in SEQ ID NO: 16 or variant thereof that differs in one or more amino acid deletions, insertions, or substitutions at no more than 15% of the residues in SEQ ID NO: 16 wherein the portion binds to phosphorylated IκB and inhibits ubiquitination of phosphorylated IκB.

3. An isolated polynucleotide that encodes a polypeptide according to claim 1, wherein the polynucleotide does not encode a full length human E3 ubiquitin ligase.

4. An isolated polynucleotide that encodes a polypeptide according to claim 2.

5. An antisense polynucleotide comprising at least 10 consecutive nucleotides complementary to a polynucleotide according to claim 3.

6. An expression vector comprising a polynucleotide according to any one of claims 3-5.

7. A host cell transformed or transfected with an expression vector according to claim 6.

8. A pharmaceutical composition, comprising:

(a) an isolated human E3 ubiquitin ligase polypeptide, wherein the polypeptide comprises a sequence recited in SEQ ID NO: 16 or a portion or variant thereof that differs in one or more amino acid insertions, deletions, additions or substitutions at no

more than 20% of the residues in SEQ ID NO:16, such that the polypeptide enhances ubiquitination of phosphorylated IκB; and

(b) a physiologically acceptable carrier.

9. A pharmaceutical composition, comprising:

(a) an isolated human E3 ubiquitin ligase polypeptide, wherein the polypeptide comprises a portion of a sequence recited in SEQ ID NO: 16, or variant thereof that differs in one or more amino acid substitutions, insertions, deletions or additions, such that the; polypeptide binds to phosphorylated IκB and inhibits ubiquitination of phosphorylated IκB; and

(b) a physiologically acceptable carrier.

10. A pharmaceutical composition, comprising:

(a) a polynucleotide encoding a human E3 ubiquitin ligase polypeptide, wherein the polypeptide comprises a sequence recited in SEQ ID NO: 16 or a portion or variant thereof that differs in one or more amino acid insertions, deletions, additions or substitutions at no more than 20% of the residues in SEQ ID NO: 16, such that the polypeptide enhances ubiquitination of phosphorylated IκB; and;

(b) a physiologically acceptable carrier.

11. A pharmaceutical composition, comprising:

(a) a polynucleotide encoding a human E3 ubiquitin ligase polypeptide, wherein the polypeptide comprises a portion of a sequence recited in SEQ ID NO: 16, or variant thereof that differs in one or more amino acid substitutions, insertions, deletions or additions, such that the polypeptide binds to phosphorylated IκB and inhibits ubiquitination of phosphorylated IκB; and

(b) a physiologically acceptable carrier.

12. A pharmaceutical composition, comprising:

(a) an antisense polynucleotide according to claim 5; and

(b) a physiologically acceptable carrier.

13. An isolated antibody, or antigen binding fragment thereof, that binds to a human E3 ubiquitin ligase sequence recited in SEQ ID NO: 16.

14. An antibody or fragment thereof according to claim 13, wherein the antibody is a monoclonal antibody.

15. A pharmaceutical composition comprising an antibody or fragment thereof according to claim 13, in combination with a physiologically acceptable carrier.

16. A method for modulating NF - κB activity in a patient, comprising administering to a patient pharmaceutical composition according to any one of claims 8-9 and thereby modulating NF - κB activity in the patient.

17. A method for treating a patient afflicted with a disorder associated with NF- κB activation, comprising administering to a patient a therapeutically effective amount of a pharmaceutical composition according to any one of claims 8-9, and thereby treating a disorder associated with NF- κB activation.

18. A method according to claim 17, wherein the disorder is selected from the group consisting of inflammatory diseases, autoimmune diseases, cancer and viral infection.

19. A method for screening for an agent that modulates NF- κB activity, comprising the steps of:

(a) contacting a candidate agent with an isolated human E3 ubiquitin ligase polypeptide, wherein the polypeptide comprises a sequence recited in SEQ ID NO:16 or a portion or variant thereof that differs in one or more amino acid substitutions, insertions,

deletions or additions, such that the polypeptide enhances ubiquitination of phosphorylated IκB, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent; and

(b) subsequently evaluating the ability of the polypeptide to enhance ubiquitination of phosphorylated IκB, relative to a predetermined ability of the polypeptide to enhance ubiquitination of phosphorylated IκB in the absence of candidate agent;

and therefrom identifying an agent that modulates NF- κB activity.

20. A method according to claim 19, wherein the candidate agent is a small molecule present within a combinatorial library.

21. A method for modulating NF - κB activity in a patient, comprising administering to a patient a polypeptide comprising a β-TrCP protein (SEQ ID NO: 18), or a portion or variant thereof that differs in one or more amino acid insertions, deletions, additions or substitutions at no more than 20% of the residues in SEQ ID NO: 18, such that the polypeptide enhances ubiquitination of phosphorylated IκB, and thereby modulating NF - κB activity in the patient.

22. A method for treating a patient afflicted with a disorder associated with NF- κB activation, comprising administering to a patient a therapeutically effective amount of a polypeptide comprising a β-TrCP protein (SEQ ID NO: 18), or a portion or variant thereof that differs in one or more amino acid insertions, deletions, additions or substitutions at no more than 20% of the residues in SEQ ID NO: 18, such that the polypeptide enhances ubiquitination of phosphorylated IκB, and thereby treating a disorder associated with NF- κB activation.

23. A method according to claim 22, wherein the disorder is selected from the group consisting of inflammatory diseases, autoimmune diseases, cancer and viral infection.

24. A method for screening for an agent that modulates NF - IκB activity, comprising the steps of:

(a) contacting a candidate agent with a polypeptide comprising a βTrCP protein (SEQ ID NO: 18), or a portion or variant thereof that differs in one or more amino acid insertions, deletions, additions or substitutions at no more than 20% of the residues in SEQ ID NO: 18, such that the polypeptide enhances ubiquitination of phosphorylated IκB, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent; and

(b) subsequently evaluating the ability of the polypeptide to enhance ubiquitination of phosphorylated I κB, relative to a predetemined ability of the polypeptide to enhance ubiquitination of phosphorylated IκB in the absence of candidate agent; and there from identifying an agent that modulates NF - κB activity.

25. A method according to claim 24, wherein the candidate agent is a small molecule present within a combinatorial library.